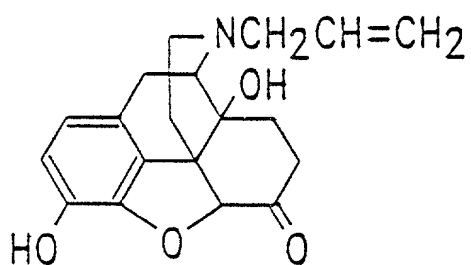
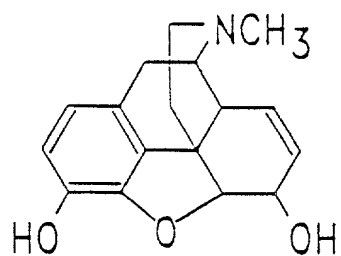
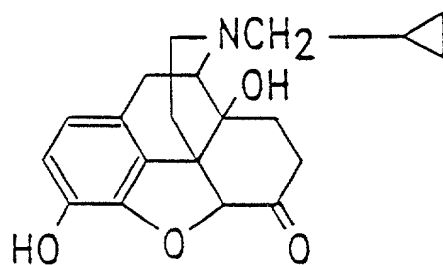


Morphine



Naloxone



Naltrexone (R=O)

Nalmefene (R=CH₂).

FIG. 1

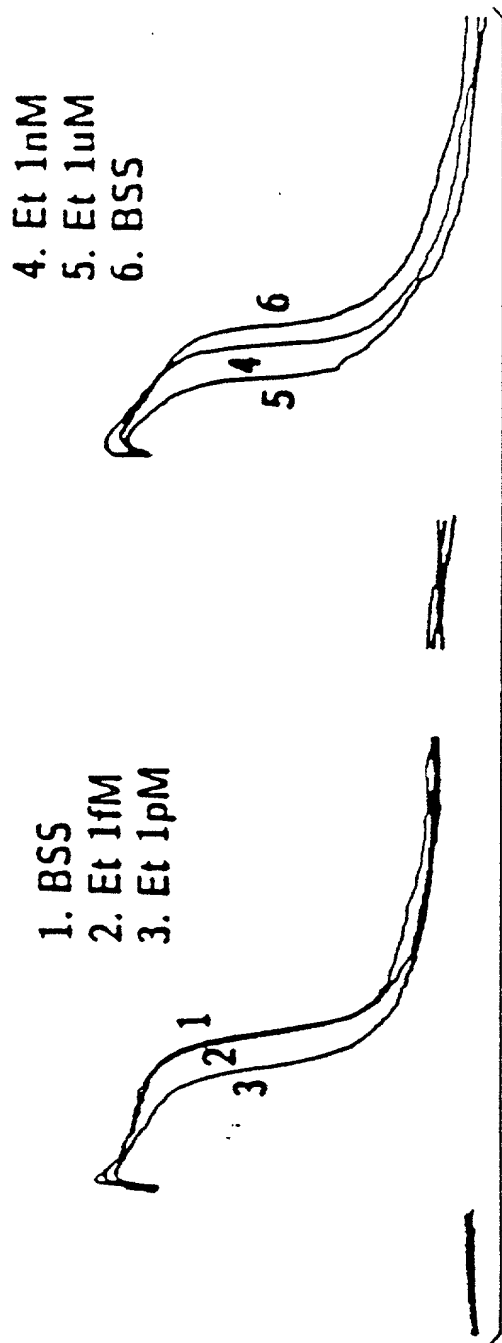


FIG. 2A

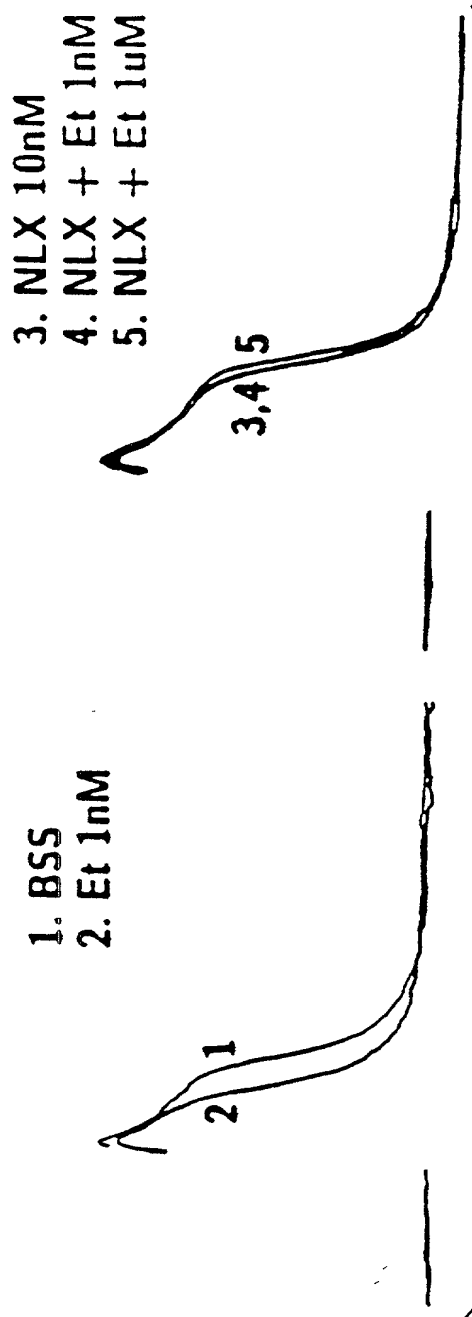


FIG. 2B

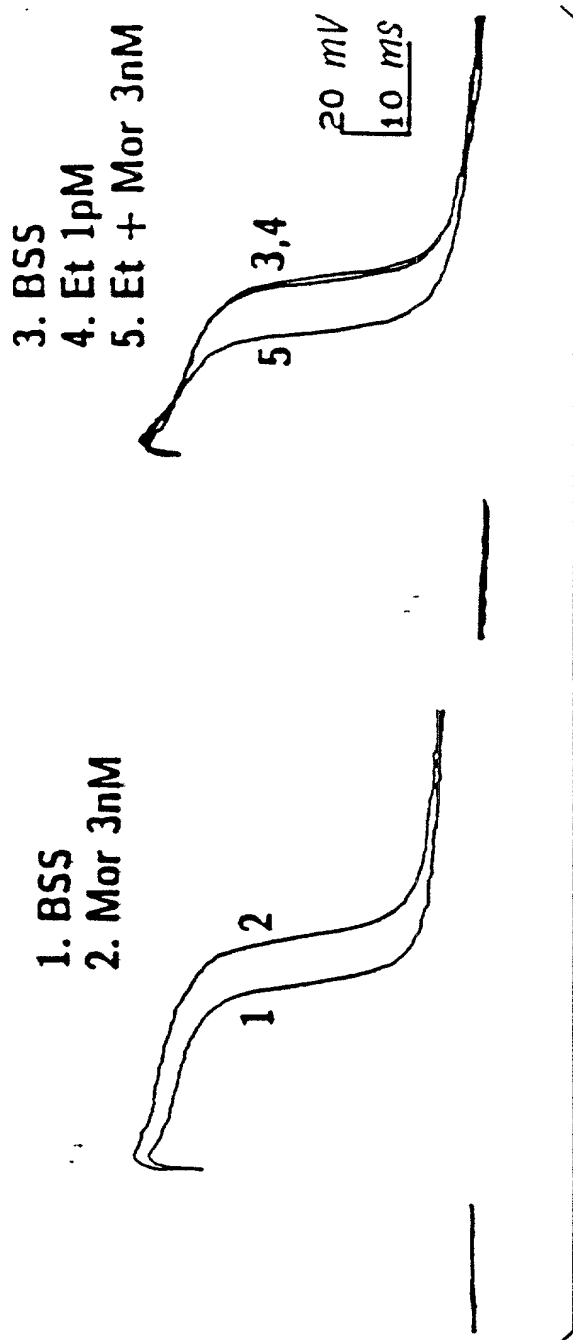


FIG. 2C

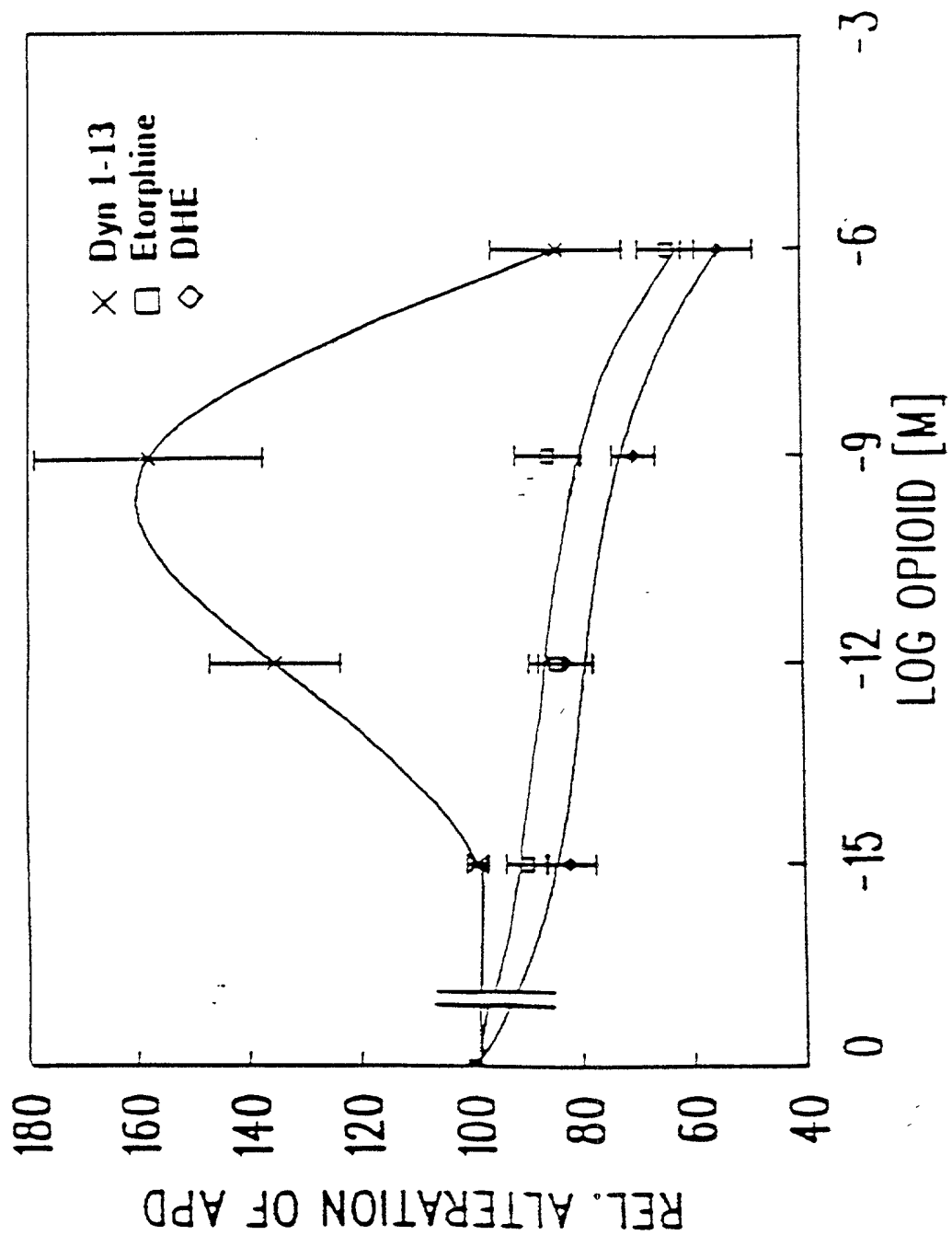


FIG. 3

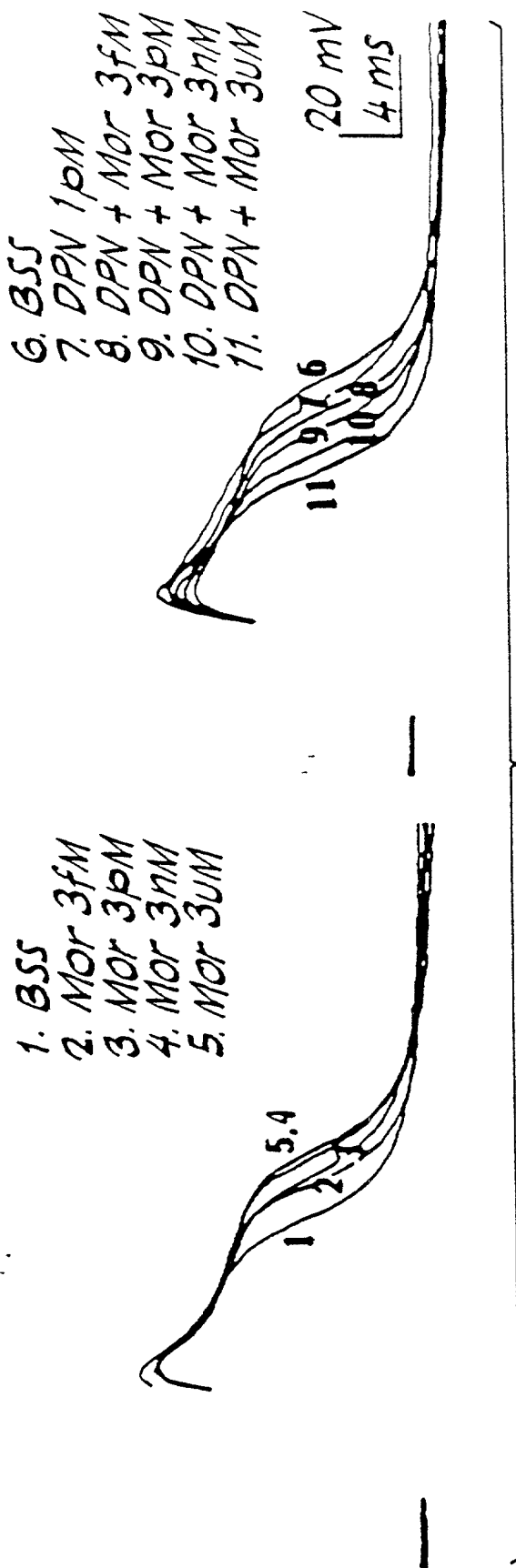


FIG. 4A

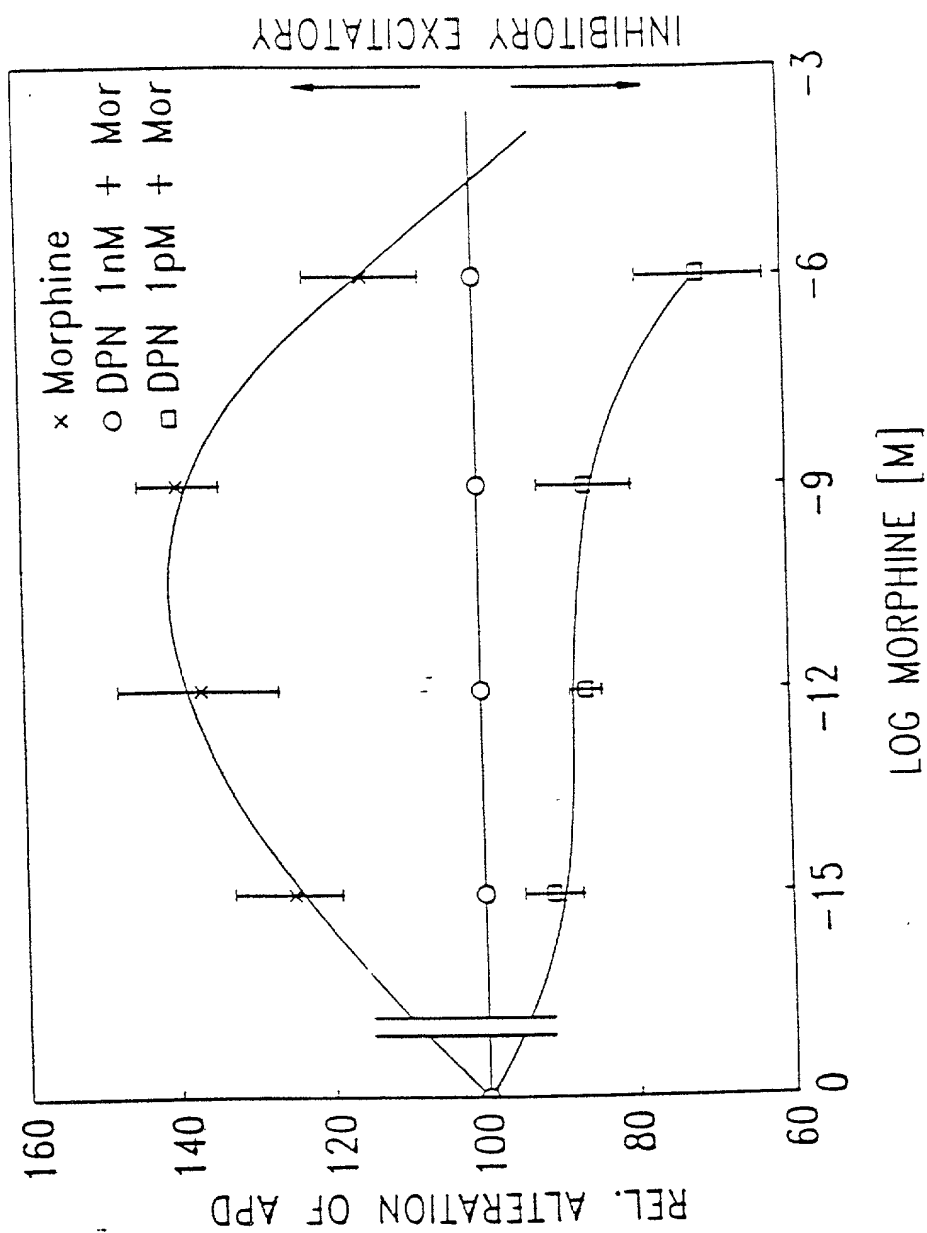


FIG. 4B.

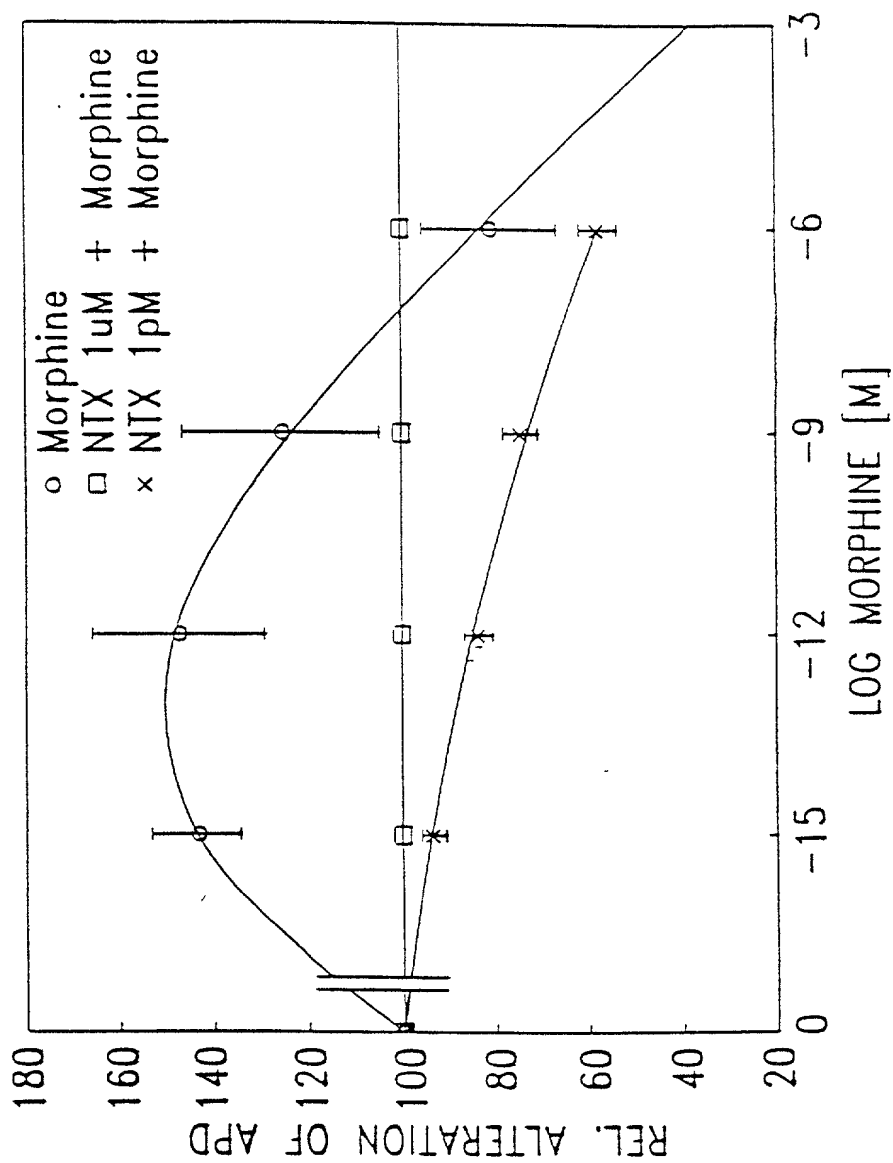


FIG. 5

Alteration of Action Potential Duration (APD)				
(APD shortening: ↓ ;APD prolongation: ↑ ;No APD change: 0)				
Acute Test	Naive DRG Neurons		Chronic Morphine-Treated Neurons (1μM; >1wk)	Chronic Co-treatment with Mor + Antag. at Excit. Op. Rec. (pM)
	Control BSS	BSS + Antag. at Excit.Op.Rec. (pM)	After Washout with BSS	
1 - 10 μM morphine	↓ (inhibitory) ("analgesia")	↑↑	↑ ("tolerance")	↑
pM - nM morphine	↓ ("excitatory antianalgesia")	↓ (unmasking of inhibitory effects)	↑	↑
~ fM morphine or dyn A-(1-13)	0	0	↑ (excitatory supersensitivity)	0
nM naloxone	0	0	↑ ("dependence") ("withdrawal effect")	0

FIG. 6

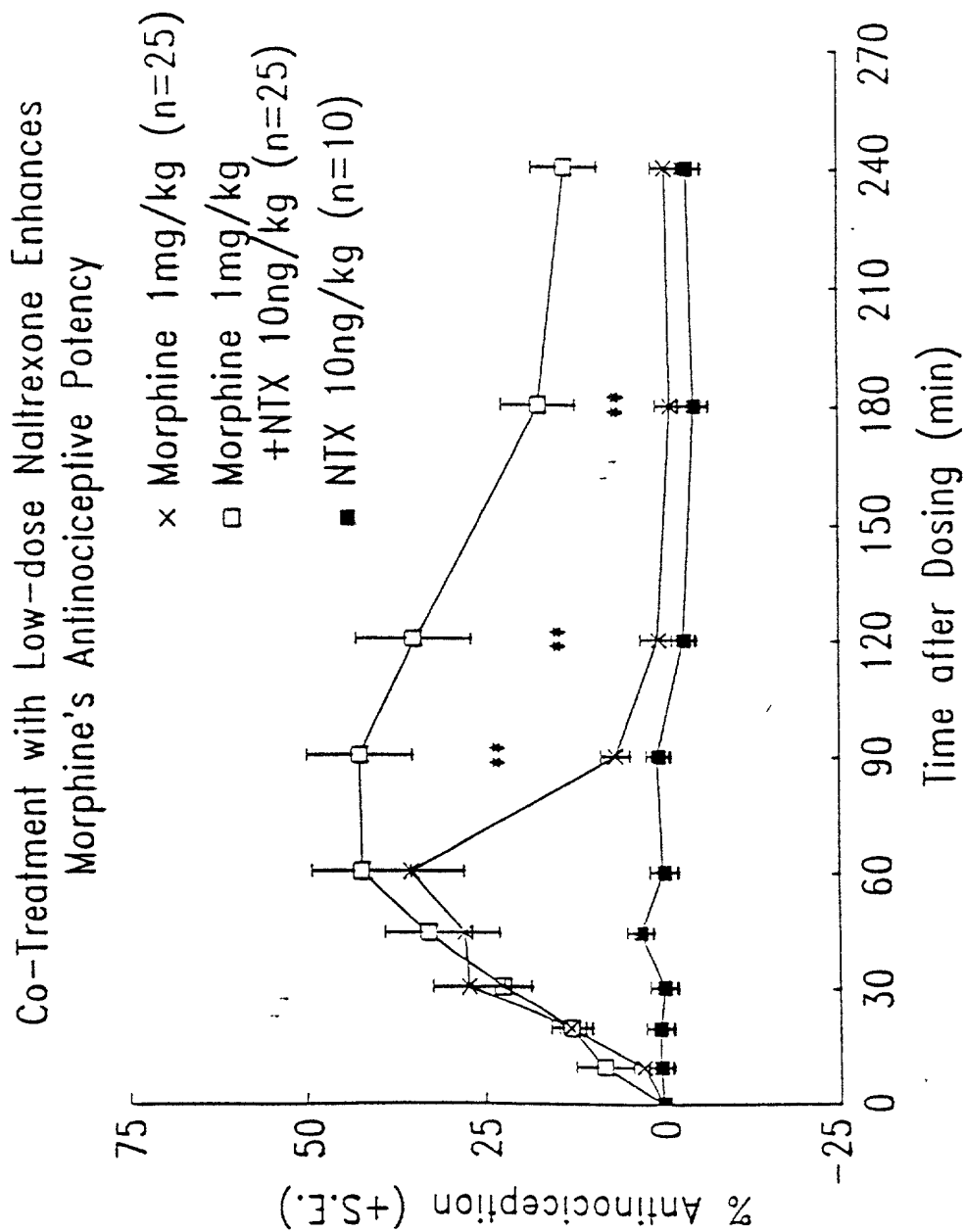


FIG. 7

Co-Treatment with Low-Dose Naltrexone Attenuates Acute and Chronic Morphine Dependence

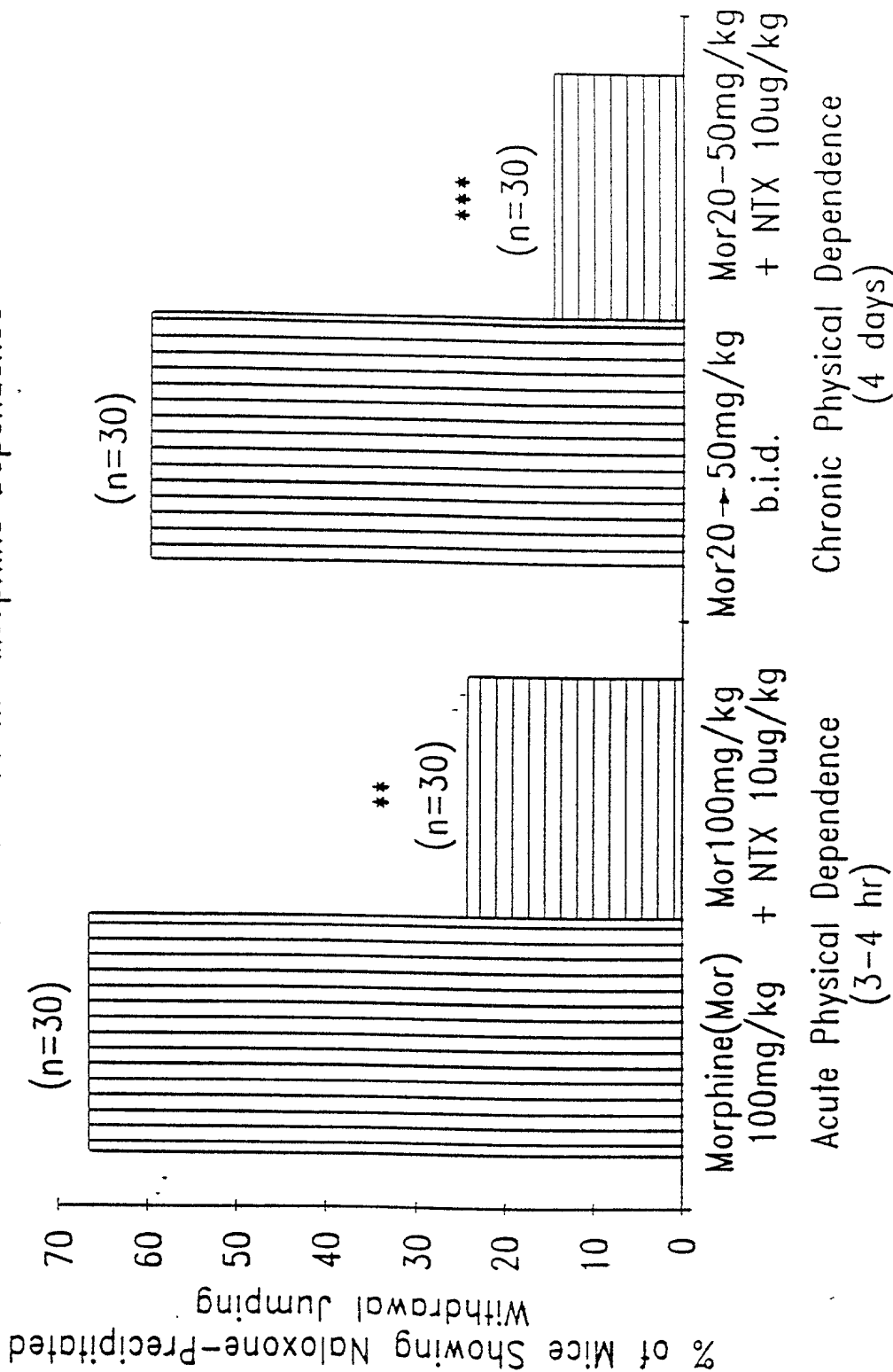


FIG. 8

Co-Treatment with Ultra-Low Dose Nalmefene Enhances Morphine Antinociceptive Potency

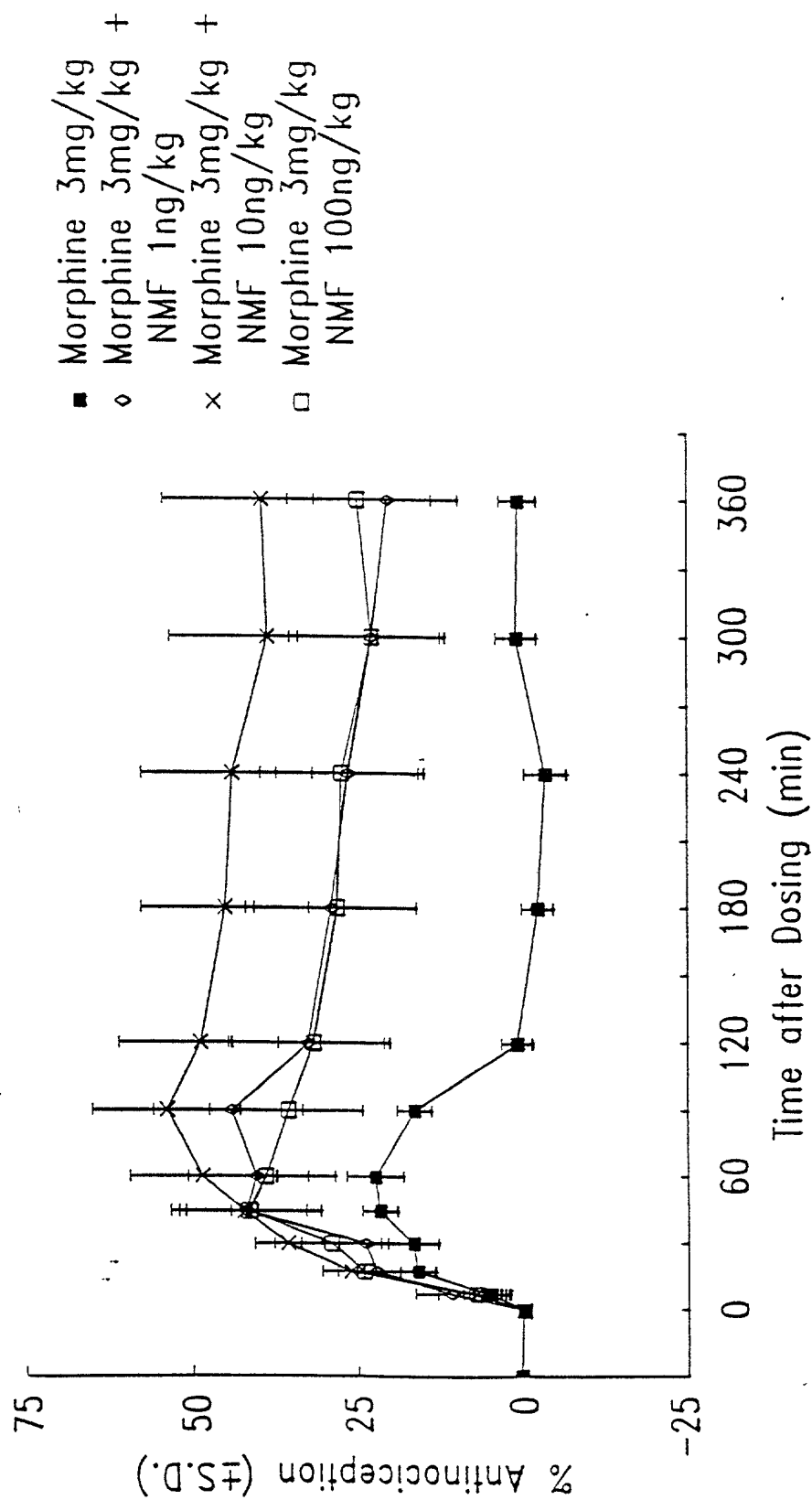


FIG. 9

Co-Treatment with Low-Dose Naltrexone or Nalmefene Attenuates Acute Morphine Dependence

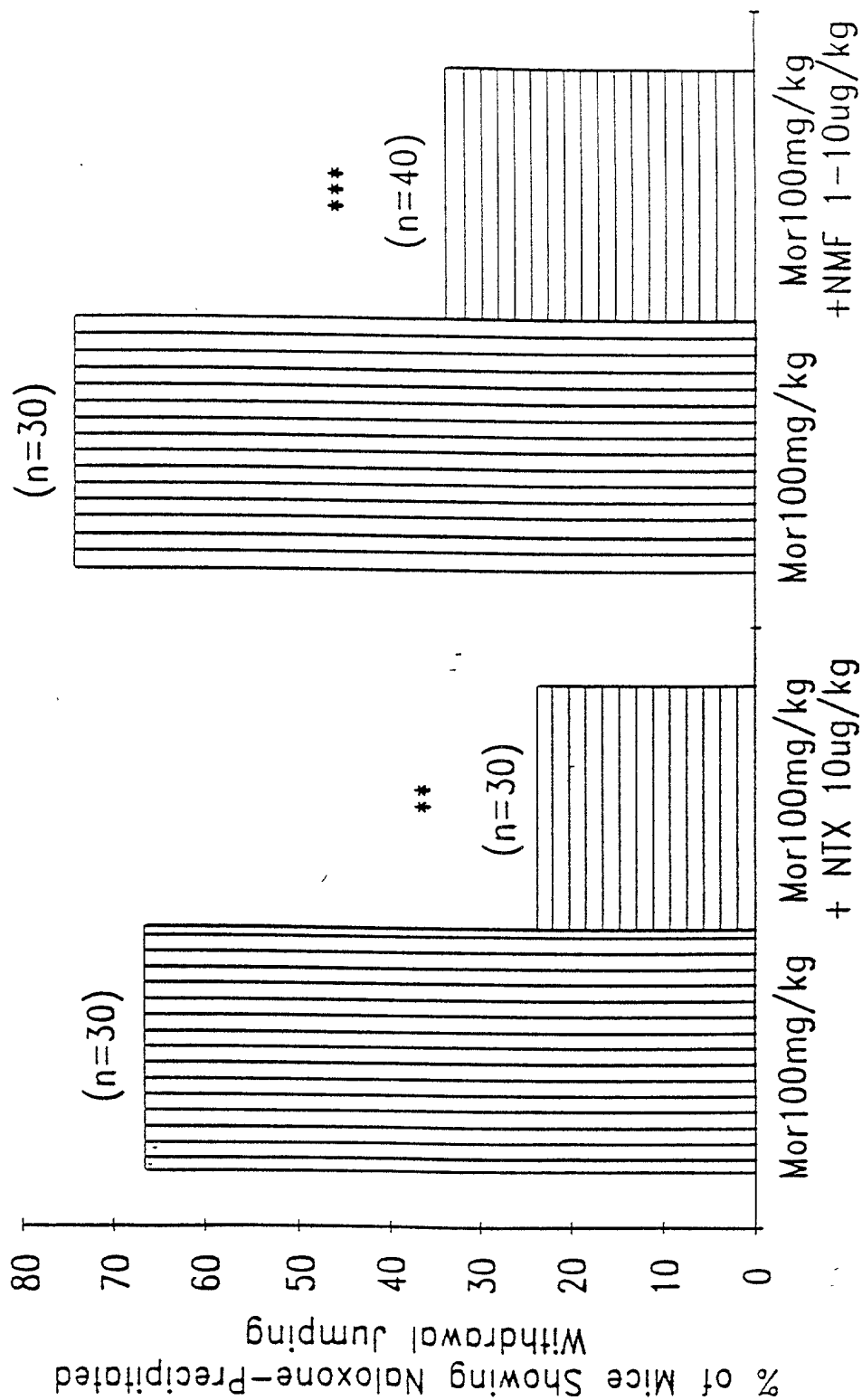


FIG. 10